Asymmetries in Chimpanzees (Pan troglodytes) Corticospinal System - A Diffusion Magnetic Resonance Imaging (MRI) Study

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Introduction: Handedness, which has been documented in captive chimpanzee at a population level [1], is likely to be associated with asymmetries in cortical motor areas and their corticospinal projections. Diffusion MRI is highly sensitive to white matter integrity and is thought to reflect the microstructure of white matter. Moreover, tractography derived from diffusion MR data is able to reconstruct major white matter pathways *in vivo*, probing both the strength and patterns of connectivity. Although primary motor cortex asymmetries in chimpanzees have been investigated using gross anatomical measures [2], no DTI study regarding this issue has been reported. In this study, diffusion MRI was used to explore chimpanzees' asymmetries in corticospinal system and their relationship with behavioral measures of handedness.

Methods: Subjects: Twenty-two female chimpanzees (age: 29 ± 15.3 yrs) were included in this study. **Behavior measures:** Handedness index (HI = (R – L)/(R + L), where R and L represent the use of right and left hand) were measured for three behaviors: simple reaching, coordinated bimanual actions (TUBE), and manual gesture [3]. **Image acquisition:** MRI images were obtained using a 3T Trio scanner (Siemens Trio, Pennsylvania, US). T1-weighted images were acquired with 3D MPRAGE sequence with the following parameters: FOV=204×204 mm^2, matrix size: 256×256, TR=2400 ms, TE=4.13 ms, 0.8 mm isotropic voxels, NEX=2; Diffusion MR data were acquired with the following parameters: segmented dual spin-echo diffusion echo-planar imaging sequence (seg=4), FOV=230×230 mm, matrix size: 128×128, TR=140 ms/slice, TE=91 ms, 41 slices covering the whole brain, 1.8 mm isotropic voxels, two averages with opposite phase encoding directions to remove the susceptibility distortion [4]. **Data analysis:** A tract-based spatial statistics routine (TBSS, FSL, /http://www.fmrib.ox.ac.uk/fsl/) was used for voxelwise asymmetry analysis [5]. In brief, the procedure is as follows: first, a symmetrical cohort-specific fractional anisotropy (FA) template was derived; then, 22 original and their left-right flipped FA images were nonlinearly registered onto the symmetrical FA template; lastly, the registered skeletons were used for a permutation test with multiple comparison corrections ($p_{FWE}<0.01$). Skeleton-based regions of interest (ROI) were extracted at four locations: the precentral gyrus (PrG), postcentral gyrus (PoG), posterior limb of internal capsule (PLIC) and superior cerebral peduncle (ScP). An asymmetry quotient (AQ=(L – R)/(L + R), where L and R represent the mean FA in the ROI in the left and right hemispheres) was calculated. The locations of the seed mask, waypoint mask and the grey matter/white matter boundary cortical mask in the probabilistic tractography study (Fdt toolbox, FSL, /http://www.fmrib.ox.ac.uk/fsl/) are shown in Fig. 1b (left). The pathways of corticospinal tracts for each chimpanzee were nonlinearly transformed to a common anatomical template and thresholded, binarized, summed and averaged to generate a variability map of the corticospinal tracts (CST) for this cohort.

Results: The TBSS results are shown in Fig. 1a. Significant left>right hemispheric asymmetries in FA were observed at PrG, PoG, PLIC and ScP. These hemispheric asymmetries were further supported by the results from the skeleton-based ROI method at these four locations (one sample t-test. PrG: t=11.68, p<0.001; PoG: t=6.5, p<0.001; PLIC: t=6.57, p<0.001; ScP: t=3.71, p<0.001). The variability map of the CSTs from the 22 chimpanzees thresholded at 60%, showing only the pathways overlapped by the majority of the individual chimpanzees, and the 3D rendition of the tracts are shown in Fig. 1b and Fig. 1c. Stronger connectivity of the CST with the precentral gyrus in the left hemisphere (AQ of strength of connectivity, Wilcoxon signed ranks test, Z=2.52, p<0.012) was detected and the location of the connectivity to the precentral gyrus is more lateral compared to that in the right hemisphere (Fig.1c). Moreover, less variability of CST at the level of PLIC was observed in the left hemisphere. A positive correlation was detected between the AQ at the PoG and the TUBE task (Pearson r = 0.6, p< 0.0029).

Conclusions: Significant hemispheric asymmetries were observed at different levels of the corticospinal system in chimpanzees. Probabilistic tractography results suggest that the asymmetry in chimpanzees' corticospinal system might be a combined result of the difference in hemispheric cortical connectivity and the asymmetry in white matter microstructure. A significant positive correlation between the AQ derived using DTI measure at the PoG and handedness indicates that the white matter microstructural asymmetry at the PoG reflects the functional lateralization of chimpanzees' corticospinal system.

References: [1]. Hopkins, W.D., et al., J. Exp. Psychol. Gen. 131(3), 412-423,2002; [2]. Hopkins, W.D., Behavioral Neuroscience, 118, 1176-1183, 2004. [3]. Taglialatela, J.P., et al., Behavior Brain Research. 184, 185-191, 2007. [4]. Andersson, J.L. , et al., NeuroImage, 20, 870-888,2003., [5]. Smith, S.M., NeuroImage. 31(4), 1487-505, 2006

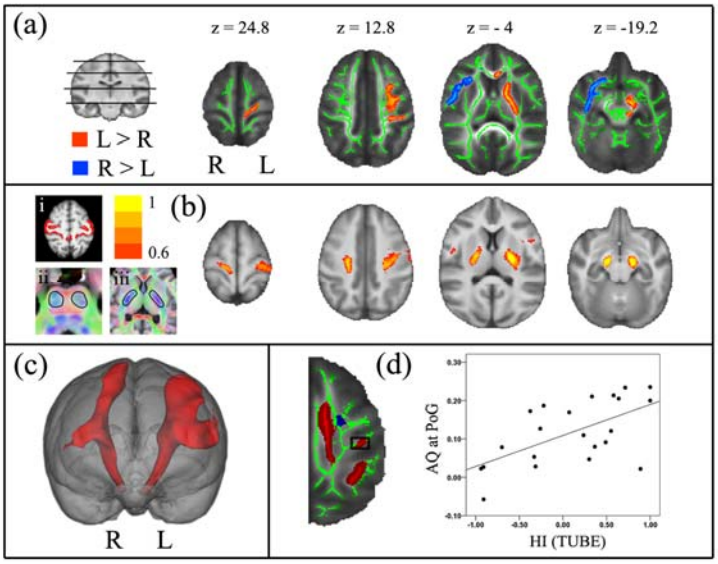

Fig.1 (a): the results from TBSS analysis. The green skeleton is overlapped on the symmetrical FA template. The differences in red represent left>right FA asymmetries; the differences in blue represent right>left FA asymmetries. (b): the results from probabilistic tractography. The left part of Fig.1b shows (i) the grey matter/white matter boundary cortical mask, (ii) the seed mask on the corticospinal tracts at the level of pons and (iii) the waypoint mask at the PLIC. The right part of Fig.1b shows the variability map of the CST of the twenty-two chimpanzees, thresholded at 0.6, showing only the part that were overlapped by the majority of the population. Fig.1c: The 3D rendition of the Fig.1b with the same threshold (60%). Fig.1d: the correlation between the AQ at the PoG and handedness index measured by using TUBE task (see results for details).